Adherence – a Delivery System Perspective

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DISCLOSURES

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Long-Term Adherence with Chronic Medications Remains a Major Problem

- **Fewer than 50% of individuals prescribed a new medication for diabetes, hypertension, or hyperlipidemia continue that drug for even a year**
- **No substantial improvement over 50 years—is this problem intractable?**

What is the "Delivery System Perspective" on Adherence?

- **Integrated systems are responsible for a population**
  - **100,000 members with hypertension and 30,000 with diabetes in KPCO, half of them non-adherent**
- **Measures need to be widely available**
- **Interventions need to be scalable (which many efficacious interventions are not)**
  - **Small effect size x broad reach = population benefit**

Are Health Care Delivery Systems Responsible for Members' Behavior?

- Medicare STAR program provides financial incentives for high quality in Medicare Advantage Plans
- Quality measures based on prescription refill adherence for oral hypoglycemics, anti-hypertensives, and lipid-lowering drugs were added in 2012
- 75% of beneficiaries need to achieve > 80% adherence for plans to receive highest quality rating
- This measure incentivizes delivery systems to take responsibility for changing patient behavior!

Efforts to Improve Adherence Are Impeded by Three Misconceptions

- Adherence is a single behavior/construct
- Socio-demographic and clinical characteristics can accurately predict adherence
- Individual clinicians can improve patient adherence on their own

Steiner, *Annals of Internal Medicine* 2012:157:580-585

Adherence is a Complex Set of Behaviors, not a Single Behavior

- The Medicare STAR program uses a measure of medication fills as its adherence metric
- Are medication fills an accurate measure of "adherence"? This is an oversimplified question!
- Adherence is a cascade of behaviors that include:
  - Seeking care
  - Keeping appointments
  - Filling a prescription
  - Taking the medication
  - Engaging in other self-care behaviors (diet, exercise, etc.)

Yearly Adherence Behaviors for a Patient with Type 2 DM, HTN, Hyperlipidemia

Behavior	Frequency	Total N/year
Diet (↓ sodium, ↓ fat)	3x daily	1095 meals
Clinician visits	Variable	4-6
Refill meds	5 meds x 4 fills yearly	20 fills
Take meds (include aspirin)	6 meds x 1-2 doses	2190 – 3650
Self-monitor BP/glucose	Variable	--
Physical activity	3-4x weekly	156 – 208 sessions
Lab/ eye exam /flu shot	4x yearly	4 contacts

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Two Cases

- **FJS is an elderly man with hyperlipidemia, coronary artery disease (bypass surgery), and other medical problems. He has taken a statin since 1990 and has achieved LDL < 100**

- **JFS is a research center director who inherited his father's lipid disorder, has taken a statin since 2006, and has achieved LDL <100**

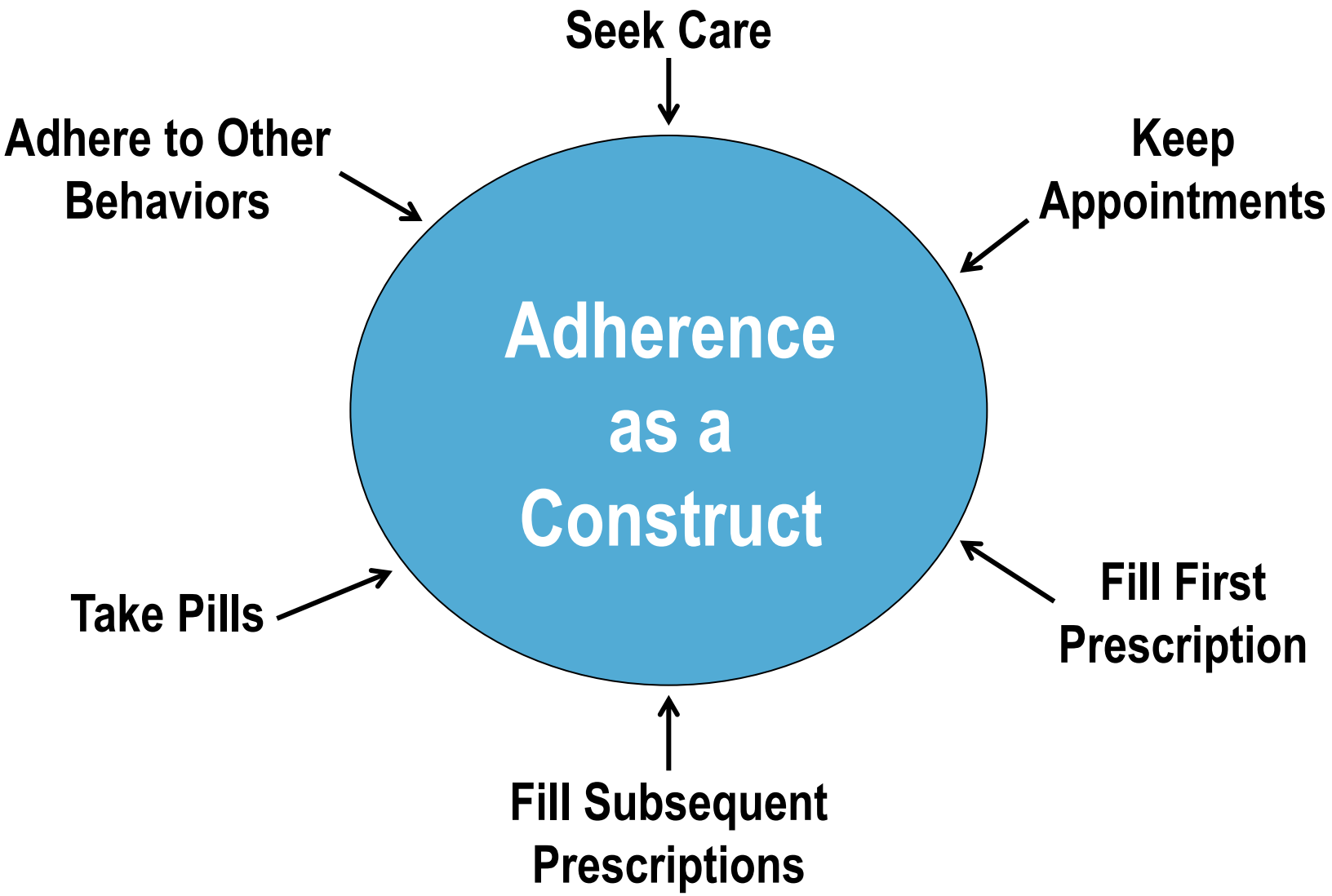
Behavior	Adherence FJS (%)	Adherence JFS (%)
Seeking Care	100% (feels secure)	50% (prefers to self-manage)
Keeping appointments	100% (gets to see the outside world)	100% (finding time is the hard part)
Filling meds	97%	97% (forgets to call pharmacy)
Taking pills	99% (uses pill organizer)	98% (misses pills when traveling)
Low-fat diet	0% (eats what he wants)	80%
Exercise	10% (limited mobility)	90%

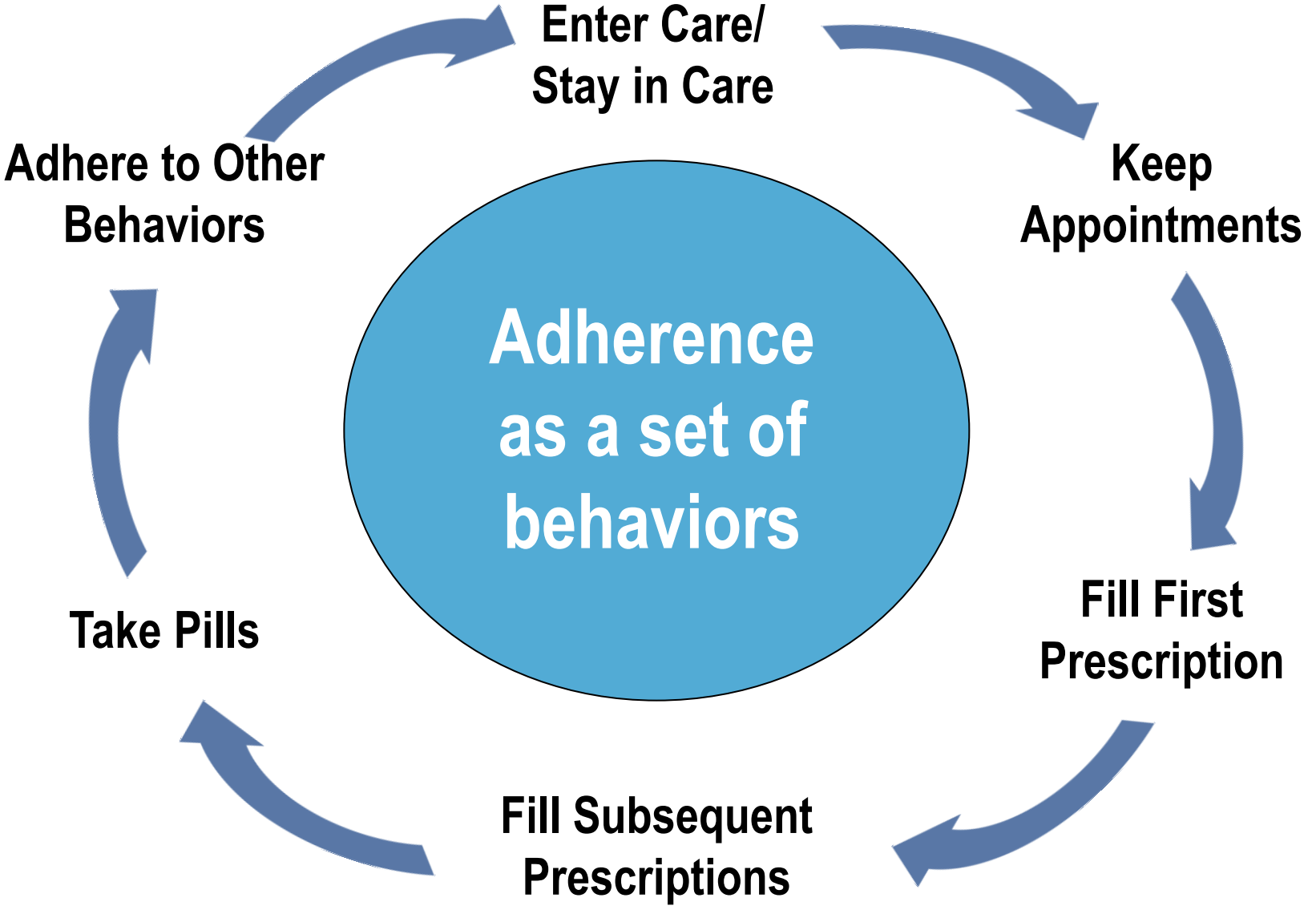
Refilling a Prescription and Taking a Pill are Not The Same Behavior!

- **JFS refill behavior: Look at label or count pills; estimate how long in advance to call pharmacy; remember to call during working hours; see doctor eventually after repeatedly pleading for new prescriptions**
- **JFS pill-taking: Store pills by toothbrush; remember to take pills on trips**

Two Cases

- Who is more “adherent”, FJS or JFS?
- Does it matter?


Seek Care
Adhere to Other Behaviors
Keep Appointments
Adherence as a Construct
Take Pills
Fill First Prescription
Fill Subsequent Prescriptions



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Implications for Adherence Research

- Arguments about “validity ” of adherence measures presume that adherence is a single construct
- Measures of different behaviors are often correlated, but may independently predict outcomes
- Which behaviors really affect outcomes? (for FJS and JFS, pill-taking trumps diet and exercise)
- Source of the “healthy adherer” effect
- Modestly effective interventions at multiple levels may lead to cumulative benefit

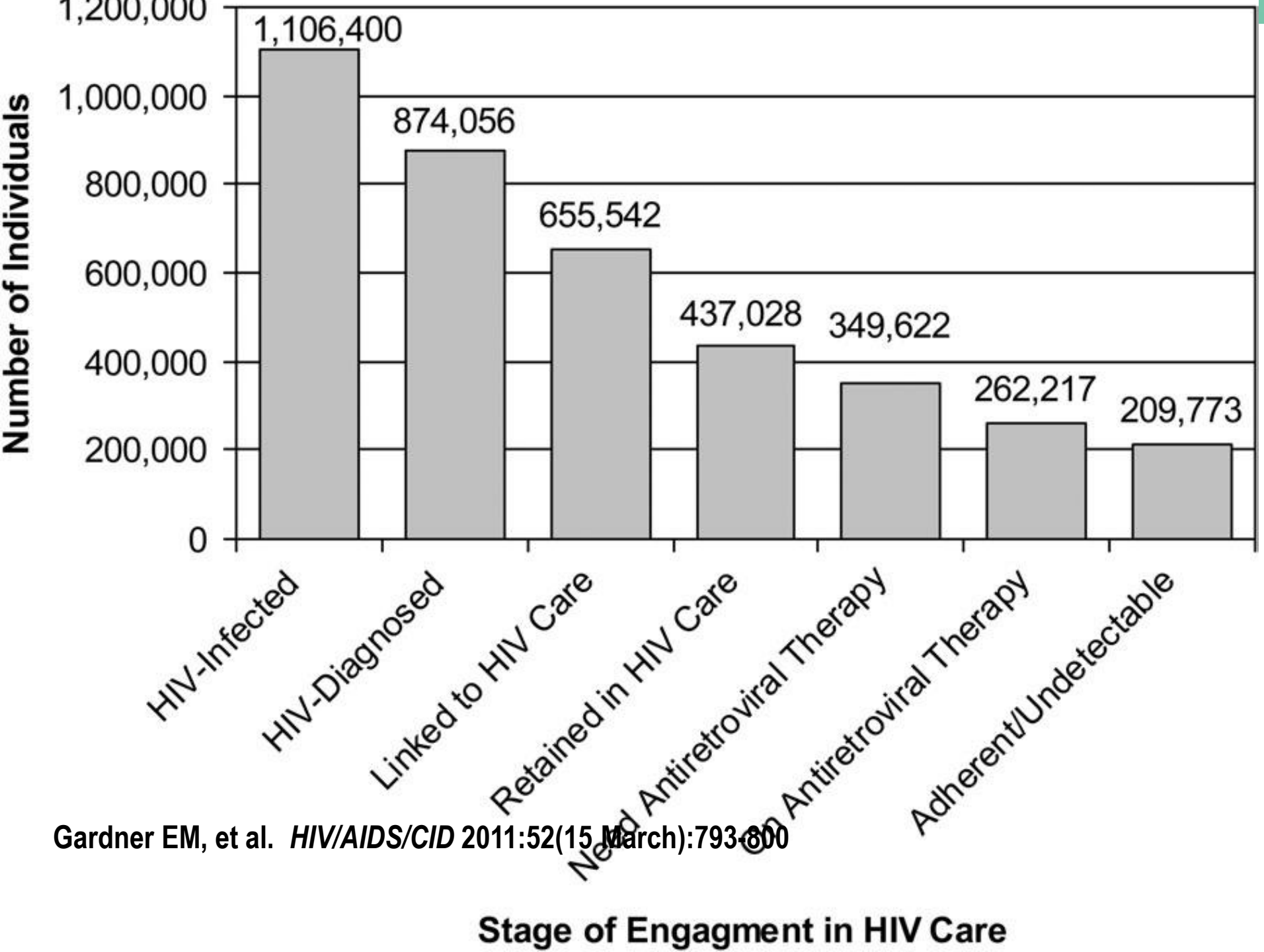
Complementary Adherence Measures

- Agreement between refill adherence and self report (kappa = 0.19, p < 0.001) (probably not the right statistic)
- In multivariate model, BP control predicted by:
  - < 80% meds obtained (OR = 0.59, 95% CI 0.38 to 0.91)
  - Self-reported non-adherence (OR = 0.65, 95% CI 0.45-0.94)

Thorpe et al, *Medical Care* 2009;47:474-81

Healthy Adherer Effect

- In a systematic review of randomized trials, high adherence with placebo is associated with lower mortality (OR = 0.56, 95% CI 0.43 to 0.74)
  - Simpson et al, *BMJ* 2006;333:15
- Adherence with statins is associated with higher adherence to PSA, FOBT, mammograms, flu shots
  - Brookhart et al, *Am J Epidemiol* 2007;166:348-354
- Responders to a medication beliefs survey are 11% more adherent with refills than non-responders
  - Gadkari et al, *Med Care* 2011;49:956-961



Gardner EM, et al. *HIV/AIDS/CID* 2011:52(15 March):793-800

Considerations for Delivery Systems

- What adherence behaviors should the system measure?
  - Measure behaviors that affect important outcomes
    - Clinical outcomes, payment (Medicare STAR)
  - Use accurate and efficient measures of those behaviors
  - Measure behaviors amenable to intervention by system
- Administrative measures: appointments, med fills
- Use of patient-reported measures is not far off

Demographic and Clinical Characteristics Cannot Accurately Predict Adherence

- Many studies have sought to identify socio-demographic predictors of adherence
- Results are inconsistent
- Individual predictors are insensitive and non-specific (odds ratios ≈ 2.0), and adherence is prevalent (≈ 50%)
- As a result, adherence differences between individuals with a "risk factor" such as minority race, mental health disorder, or substance use and those without are not actionable!

Strategies to Target Individuals Predicted to be Non-adherent are Misguided

- Predictive models are all the rage
- However, need to assess the extent of misclassification and the "costs" of misclassification
- Cost of a "false positive" (adherent despite an adverse predictor)—labeling, bias, differential treatment
- Cost of a "false negative" (non-adherent despite favorable predictors)—missing an opportunity to intervene

Sociodemographic Predictors of Adherence: An Illustration of Flawed Clinical Reasoning

	Adherent? No	Adherent? Yes	
Sociodemographic Predictors Present	136	64	200
Sociodemographic Predictors Absent	364	436	800
	500	500	1000

Assumptions:
1. Prevalence of non-adherence is 50%
2. Prevalence of potential predictor is 20%
3. Relative risk of potential predictor is ~ 2.0

Calculations:
Relative risk of predictor = 2.1
Sensitivity of predictor = 0.27 Specificity of predictor = 0.87
Prior probability of non-adherence = 50%
Probability of non-adherence in presence of predictor (PV+) = 68%
Probability of non-adherence in absence of predictor (1-PV-) = 46%

Do Physicians' Predictions of Adherence Affect Treatment Recommendations?

- National survey of HIV providers and patients (1996-8)
- 89% of physicians said that likelihood of adherence affected their treatment decisions for HIV meds
- "Selective" providers prescribed HIV meds later to women, Latinos, and poor people than to men, whites, or those with higher income
- All providers prescribed later for African-Americans than for whites

Wong, *J Gen Intern Med* 2004;19:366-74

Considerations for Delivery Systems

- Risk models to predict adherence from currently available patient-level socio-demographic and clinical information will not prove useful and may do harm
- Will "big data" analytics allow accurate prediction of adherence?
  - Patient attitudes have been stronger predictors of adherence in many studies, but difficult to collect at large scale
  - Other contextual sources?
- But why not just measure adherence directly?

Improving Adherence is a "Team Sport", Not the Sole Responsibility of Front-line Clinicians

- Office-based counseling by clinicians can produce modest improvements, but intensive, hard to initiate, and sustain
- Outreach (e.g., disease management in person or using technology) can also be effective, but requires coordination with clinical care.
- System-based and policy interventions can affect adherence at population level

Examples of System-level Adherence Interventions

- Eliminate Medicare “donut hole”
- Reduce/eliminate copayments for essential drugs
- Use of mail-order pharmacy services
- Dispense large (90-day) rather than small (30-day) refills

Medicare Part D "Donut Hole" and Adherence

- Coverage gap for Medicare beneficiaries who spend more than a threshold amount on medications
- KPCO study found that adherence fell by 3-8 percentage points after Medicare patients reached the threshold
  - Raebel et al. Med Care 2008; 46:1116-1122.
- Many other studies have confirmed this finding
- Legislators can improve adherence by abolishing the donut hole before 2020!

Reducing Cost Barriers Can Improve Adherence (Choudhry, *NEJM* 2011)

- Eliminated copayments for essential meds after myocardial infarction (in a RCT)
- Refill adherence increased by 4-6 percentage points
- No change in subsequent rate of first major vascular events/revascularization, costs
- Significant reduction in vascular endpoints (rate of total events)

Choudhry, NEJM 2011;365:2088-97

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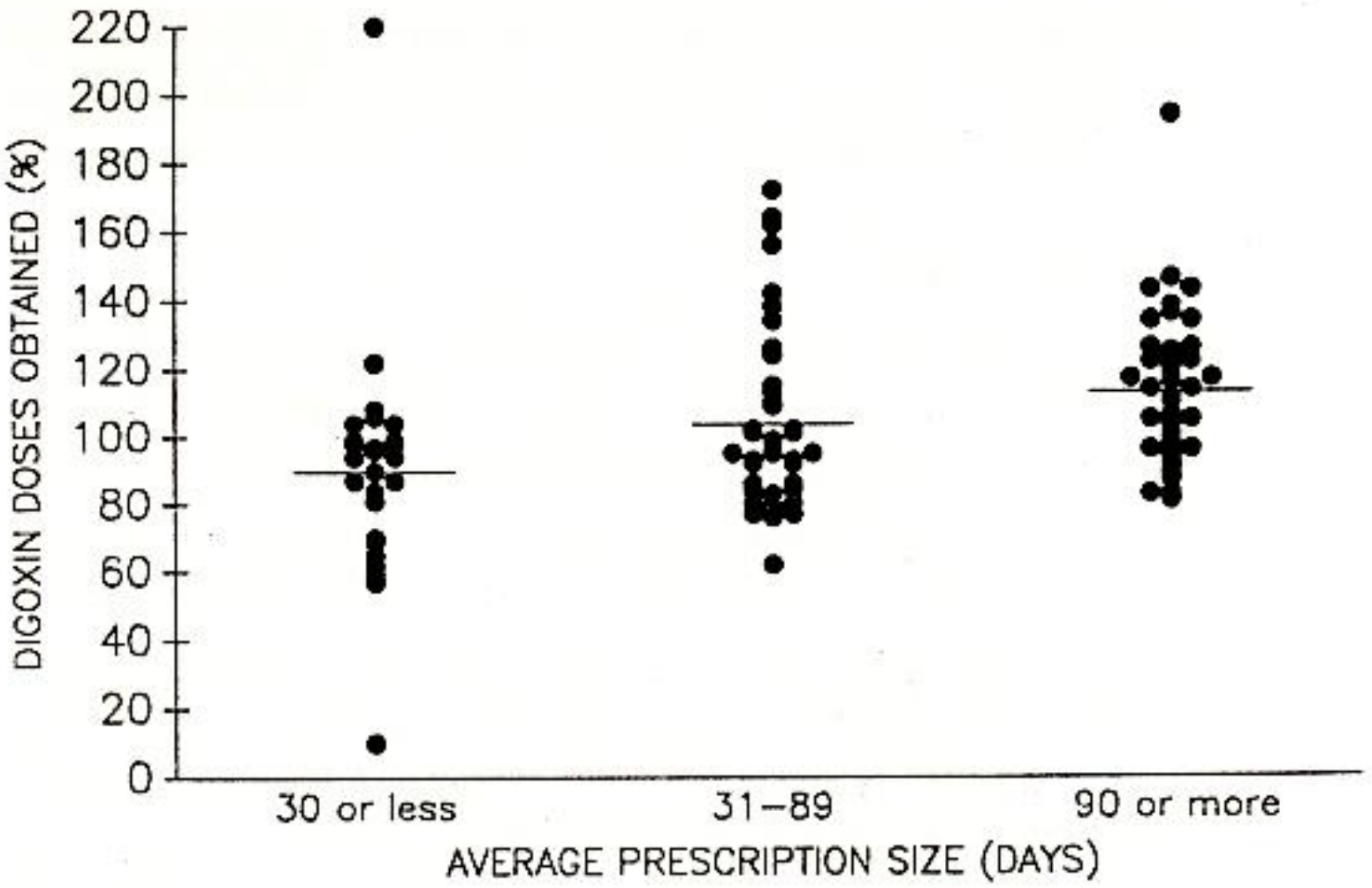
Mail Order Pharmacy Use, Adherence, and Risk Factor Control

- KPNC members who obtained mail-order refills of statins were more adherent (88% vs. 73%) and more likely to achieve LDL control (85% vs. 74%)
  - Schmittdiel et al, *J Gen Intern Med* 2011;26:1396-1402.
- Although minority KPNC members had lower adherence with new BP meds, disparities lessened after accounting for copayment, mail order use
  - Adams et al, *Arch Intern Med* 2013; 173:54-61

Relationship between prescription size and adherence



Steiner JF, *J Gen Intern Med 1993;8:306-320*

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Prescription Size, Adherence, and Clinical Outcomes

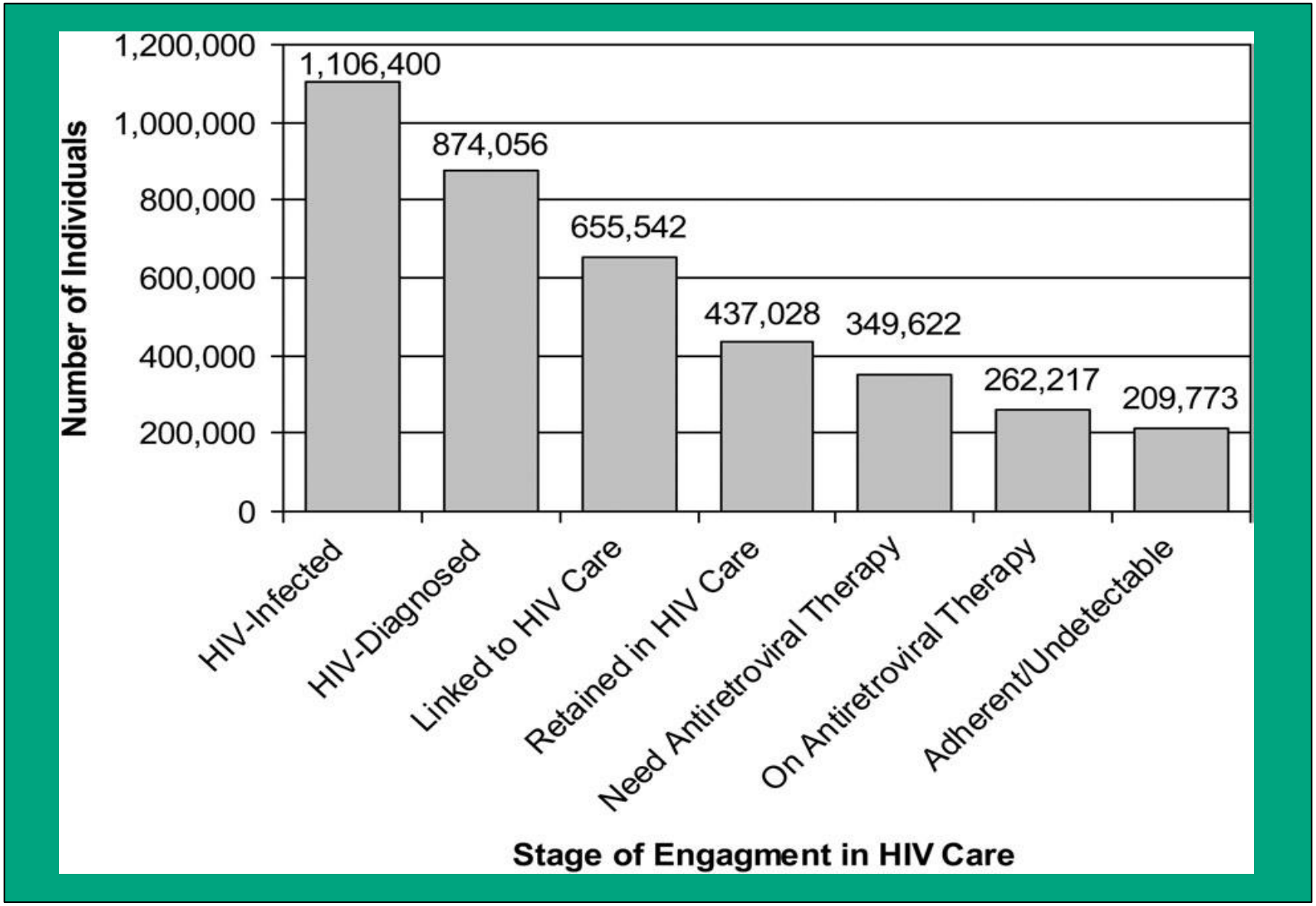
- 60-day statin supplies were associated with higher adherence and lower LDL cholesterol levels than 30-day supplies
  - Batal et al, *BMC Health Serv Res.* 2007;7:175
- 1-year supplies of oral contraceptives were associated with lower rates of unintended pregnancy
  - Foster DG et al, *Obstet Gynecol.* 2011;117:566-76

Considerations for Delivery Systems

- Delivery systems have the capacity to "nudge" changes in adherence behavior in several ways
  - Reducing out-of-pocket costs (coverage gaps, copays)
  - Enhancing convenience (larger supplies, mail-order pharmacy)
  - Brief motivational messages about adherence
    - Rinfret S et al, *Heart* 2013;99:562-569
  - Refill reminder calls
    - Ho et al, *JAMA Intern Med* 2014;174:186-193

Useful Directions for System-Based Adherence Research

- "Dashboards" to monitor adherence cascade at population level
- Point-of-care, self-reported measures of medication taking and barriers to adherence
- E-health or M-health outreach interventions
- Establish adherence/outcome relationships—is the 80% adherence threshold clinically justified?



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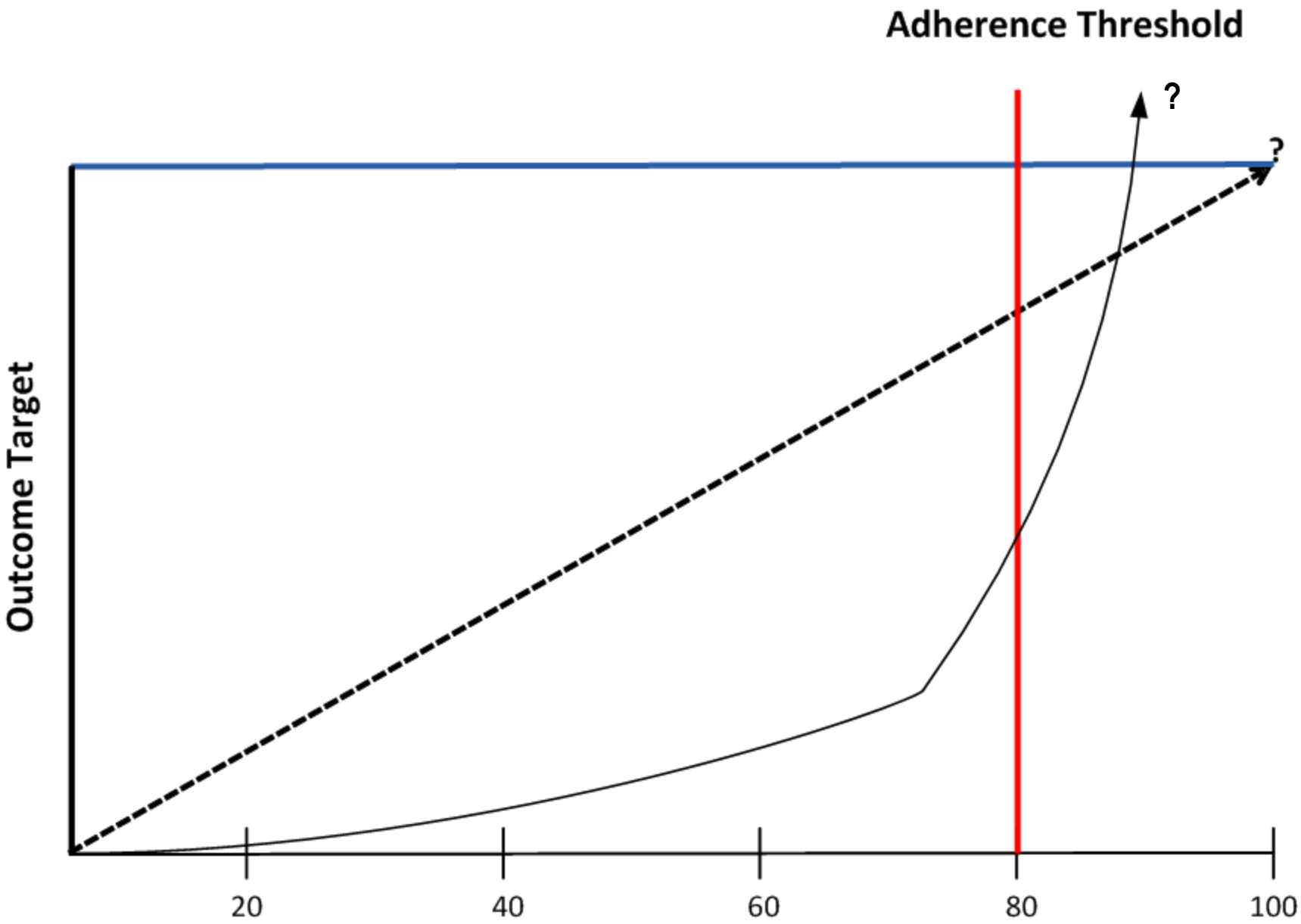

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Adherence in Delivery Systems – Final Thoughts

- System-level interventions may be least expensive per person, most scalable and most sustainable
- Effect of high-deductible plans on multiple adherence behaviors
- Can the primary care medical home improve adherence?
- Coordination of office, outreach, and system-level interventions requires communication and informatics tools
- High adherence at the population level is possible: several organizations have reached Medicare STAR adherence goals